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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/846,346	04/30/2001	George Jackowski	2132.013	3157

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EXAMINER	
GABEL, GAILENE 13	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/846,346	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 30 December 2002 .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-35 is/are pending in the application.

4a) Of the above claim(s) 1,2 and 29-35 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 3-28 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-35 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5,11 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II, claims 3-28, without traverse, filed 12/30/02 in Paper No. 12 is acknowledged and has been entered. Claims 1-2 and 29-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Accordingly, claims 1-35 are pending. Claims 3-28 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 3-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is vague and indefinite in reciting, "evidencing", first, second, and third occurrence, because it is unclear what Applicant intends to encompass in such a recitation. Perhaps Applicant intends "confirming the presence of (a disease state or a biopolymer marker)". See also claims 4 and 5.

Claim 3 is vague and indefinite in reciting, "biopolymer marker sequence or analyte thereof", first and second occurrence, because it is unclear how an element is an analyte of a biopolymer marker. See also claim 4. Additionally, claim 3 lacks

antecedent support in reciting, "(biopolymer marker sequence or analyte thereof) isolated from said sample" because it is unclear how the biopolymer marker was isolated from the sample using spectrophotometric analysis, i.e. selective characteristic molecular weight, amino acid sequence, etc.

Claim 3 is vague and indefinite in reciting, "comparing said at least one isolated biopolymer marker ... to the biopolymer marker sequence as set forth in claim 1" because it is unclear what property or element of the isolated biopolymer marker is compared to that of SEQ ID NO. 1 in claim 1.

Claim 3 is ambiguous in reciting, "wherein correlation of said isolated biopolymer marker and said biopolymer marker sequence as set forth in claim 1 evidences and categorizes said at least one disease state" because it is unclear how these two elements are correlated so as to provide confirmation of the presence a disease state, i.e. presence, decrease, increase, absence of one marker in relation to the other.

Claim 4 is indefinite in reciting, "particularly" because the term, "particularly" is a subjective term that lacks a comparative basis for defining its metes and bounds. See also claim 5.

Claim 4 is confusing because it is unclear what functional cooperative relationship exists between the recitation of, "directed to biopolymer markers or analytes thereof linked to at least one risk of disease development" and the "at least one isolated biopolymer marker sequence" (which is SEQ ID NO. 1) recited in claim 3. Is there more than one biopolymer marker sequence involved.

Claim 5 is confusing because it is unclear what functional cooperative relationship exists between the recitation of, "directed to biopolymer markers or analytes thereof related to the existence of a particular disease state" and the "at least one isolated biopolymer marker sequence" (which is SEQ ID NO. 1) recited in claim 3. Is there more than one biopolymer marker sequence involved.

Claim 10 is vague and indefinite in reciting, "biopolymer marker or analyte thereof", first and second occurrence, because it is unclear how an element is an analyte of a biopolymer marker. See also claim

Claim 10 is indefinite in failing to recite a positive limitation in the claim in reciting, "capable of".

Claim 11 has improper antecedent basis problem in reciting, "said biochemical material or biomolecule". Perhaps, Applicant intends, "said biochemical material or said biomolecule".

Claim 12 is vague and indefinite in relation to claim 10 from which it depends in reciting, "at least one labeled biochemical material" because it is unclear as to whether the biochemical material in the instant claim is the same as the biochemical material recited in claim 10, but including a label. Perhaps, Applicant intends the labeled biochemical material to be a second biochemical material that is conjugated to a label. See also claim 14.

In claim 17, "therefore" should be --therefor--.

Claim 18 is indefinite in failing to recite a positive limitation in the claim in reciting, "capable of".

Claim 18 is vague and indefinite in reciting, "biopolymer marker ... or analyte thereof", first and second occurrence, because it is unclear how an element is an analyte of a biopolymer marker. See also claim 25.

Claim 18 is confusing in reciting, "at least one analysis to determine a presence of ... a biochemical material" because the assay kit appears to be drawn to its use in determining the presence of a biopolymer marker using the biochemical material, and not to determining the presence of the biochemical material, i.e. antibody, specific thereto. Alternatively, it is unclear what structural and functional cooperative relationship exists between "a biochemical material" (second occurrence in the claim) and "at least one biochemical material" (first occurrence in the claim).

Claim 19 has improper antecedent basis problem in reciting, "said biochemical material or biomolecule". Perhaps, Applicant intends, "said biochemical material or said biomolecule".

Claim 20 is vague and indefinite in relation to claim 18 from which it depends in reciting, "at least one labeled biochemical material" because it is unclear as to whether the biochemical material in the instant claim is the same as the biochemical material recited in claim 18, but including a label. Perhaps, Applicant intends the labeled biochemical material to be a second biochemical material that is conjugated to a label. See also claim 22.

Claim 21 lacks clear antecedent support in reciting, "said biochemical material" since claim 18 appears to recite more than one "biochemical material". See also claim 25.

In claim 25, "therefore" should be --therefor--.

Claims 26-28 are confusing because they depend from and are intended to be drawn to an "an assay kit" but the limitations set forth in these claims appear to be drawn to a method. Please clarify.

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 3-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a method for evidencing and categorizing at least one disease state by obtaining a sample from a patient, subjecting the sample to mass spectrophotometric analysis, isolating and identifying a biopolymer marker that correlates to a biopolymer marker having a sequence identified as SEQ ID NO. 1, the presence of which is indicative of the presence of an at least one disease state.

The state of the prior art- the prior art of record fails to disclose a method for evidencing and categorizing Type II diabetes as an at least one disease state, by obtaining a sample from a patient, subjecting the sample to mass spectrophotometric analysis, isolating and identifying a biopolymer marker which consists of SEQ ID NO. 1, the presence of which is indicative of the presence of Type II diabetes as the at least one disease state (specification at page 27, line 17 to page 28, line 2).

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the claimed method which shows isolation and identification of any biopolymer marker, which correlates to SEQ ID NO. 1, specifically supports diagnosis or indication of Type II diabetes.

The amount of direction or guidance present- the specification fails to provide any guidance to enable the claimed method to evidence and categorize an isolated and identified biopolymer marker which correlates to SEQ ID NO. 1 to be diagnostic or indicative of a specific disease state such as Type II diabetes.

The presence or absence of working examples- there are no working examples that show data and results wherein isolation and identification of any biopolymer marker

which correlates to SEQ ID NO. 1, including the marker which is isolated and identified as SEQ ID NO. 1 in the specification at page 27, line 17 to page 28, line 2, specifically supports diagnosis or indication of Type II diabetes.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the method as claimed based on the instant specification.

*The relative skill of those in the art-*the level of skill in the art is high.

The breadth of the claims- as recited, the instant claims are directed to a method for evidencing and categorizing at least one disease state by obtaining a sample from a patient, subjecting the sample to mass spectrophotometric analysis, isolating and identifying a biopolymer marker that correlates to a biopolymer marker having a sequence identified as SEQ ID NO. 1, the presence of which is indicative of the presence of at least one disease state.

In page 6, lines 5-13, Applicant provides that biopolymers or analytes thereof include but are not limited to proteins, peptides, DNA, RNA, carbohydrates, steroids, and lipids. At page 12, lines 1-17 of the specification, Applicant discusses that SELDI-MS and time-of-flight (TOF) detection procedures are used to maximize the diversity of the biopolymers which are verifiable within a particular sample and then analyze their ability to evidence a disease state to enable diagnosis of the presence or absence of an at least one disease state relative or which correlates, to the presence or absence of a particular biopolymer marker. In pages 12-16 of the specification, Applicant states numerous biopolymer markers associated with diseases of the complement system, i.e.

the major effector of the humoral branch of the immune system (C3 deficiency-recurrent bacterial infection and autoimmune reactions, etc.), and the Syndrome X continuum, i.e. multifaceted syndrome (insulin resistance/hyperinsulinemia, dyslipidemia, hypertension, obesity, glucose intolerance, non-insulin dependent diabetes mellitus, etc). At page 27, line 17 to page 28, line 2, Applicant provides that a specific disease specific marker which is SEQ ID NO. 1, which is characterized as a C3f fragment from the complement system having a molecular weight of about 1998 daltons has been isolated and identified using the claimed method. Applicant states that a deduction from the data set forth in Figure 1, supports that this biopolymer marker having SEQ ID NO. 1, is indicative of Type II diabetes as the at least one disease state. However, nowhere in the specification including Figure 1 and Figure 2, supports the assertion that SEQ ID NO. 1 is indicative of or diagnostic of Type II diabetes. Nowhere in the limited disclosure provides a description of how the biopolymer having SEQ ID NO. 1 is diagnostic of or indicative of Type II diabetes based on characterization of the disease, i.e. symptomatic or asymptomatic, and manifestation of the biopolymer having SEQ ID NO. 1. in a patient sample. There is no evidentiary showing, given the instant specification and data obtained from Figure 1, that one skilled in the art would have deduced that a patient having a biopolymer marker having SEQ ID NO. 1, would have been specifically evidenced and categorized as diagnostically having Type II diabetes. There is no description as to whether this protein having 17 amino acids in length is the reactive marker that is diagnostic of Type II diabetes, or that a reactive fragment comprising a stretch of amino acid positions within SEQ ID NO. 1 is diagnostic of or

indicative of Type II diabetes. Alternatively, the prior art reference Capiaumont et al., teach SEQ ID NO. 1 which is C3f (SSKITHRIHWESASLLR), a fragment of human complement containing HWESAS motif which Capiaumont et al. describes as a biopolymer which exhibits, i.e. evidences or categorizes, at least one disease state; in this case, chronic renal failure, which is not in any way related to the same organ system as is involved in Type II diabetes.

In as far as the claims, claims 3, 10, and 18 recite, "evidencing and categorizing at least one biopolymer marker sequence or analyte thereof [that is] isolated and identified to be correlated to a biopolymer marker having a sequence identified as SEQ ID NO. 1, and wherein a correlation therebetween evidences or categorizes at least one disease state. However, the specification fails to provide a description of how the at least one biopolymer marker isolated and identified from the patient sample is correlated to the biopolymer marker having SEQ ID NO. 1. The specification does not define how or otherwise show, what element of the biopolymer protein structure isolated from the patient sample, such as amino acid structure, molecular weight, reactivity of the full length sequence protein or reactive fragment thereof, physiological function, etc., correlates to the biopolymer having a sequence identified as SEQ ID NO. 1. Alternatively, the specification discloses numerous disease states that can be identified by the claimed method and therefore, it is not clear in the instant claims 3-28 as to what particular disease state is evidenced and categorized by the isolation and identification of the biopolymer marker that is correlated to the biopolymer marker having a sequence identified as SEQ ID NO. 1. Further, there are no working examples that would lead

one skilled in the art to arrive to the identification of SEQ ID NO. 1 in the specification, as a specific diagnostic marker that provides indication of an at least one disease state, in this case, specifically Type II diabetes as set forth in Figure 1.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue. It has been set forth above that 1) the experimentation required to enable the isolation and identification of any biopolymer marker which broadly correlates to a biopolymer having a sequence identified as SEQ ID NO. 1, which evidences, categorizes or supports diagnosis and indication of Type II diabetes, would be great as 2) there is no experimental evidence provided that would indicate that the claimed method would work to identify an at least one disease state, such as Type II diabetes, using a biopolymer marker that is correlated to a biopolymer marker having a sequence identified as SEQ ID NO. 1; 3) there is no proper guidance that shows that the claimed method can evidence and categorize an isolated and identified biopolymer marker which correlates to a biopolymer marker having a sequence identified as SEQ ID NO. 1, to be diagnostic or indicative of a specific disease state such as Type II diabetes, 4) the nature of the invention is a method for evidencing and categorizing at least one disease state by obtaining a sample from a patient, subjecting the sample to mass spectrophotometric analysis, isolating and identifying a biopolymer marker that correlates to a biopolymer marker having a sequence identified as SEQ ID NO. 1, the presence of which is indicative of the presence of at least one disease state, 5) the relative skill of those in the art is high, yet 6) the state of the prior art has been shown to be unpredictable as

evidenced by the fact that no prior art has been cited that shows a biopolymer marker isolated and identified by the claimed method as having a sequence identified as SEQ ID NO. 1 that evidences or categorizes a disease state to be specifically diagnostic or indicative of Type II diabetes, and lastly 7) the claims broadly recite a method for evidencing and categorizing at least one disease state by obtaining a sample from a patient, subjecting the sample to mass spectrophotometric analysis, isolating and identifying a biopolymer marker that correlates to a biopolymer marker having a sequence identified as SEQ ID NO. 1, the presence of which is indicative of the presence of at least one disease state.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 3-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hutchens et al. (US 6,225,047) in view of Capiaumont et al. (Assay of seric human hexapeptide (HWESAS) using a monoclonal antibody and ELISA, Clinica Chimica Acta 293: 89-103 (2000)).

Hutchens et al. disclose a method and kit for identifying biopolymer markers (diagnostic markers) representative of or capable of categorizing specific disease states using Surface Enhanced Laser Desorption Ionization Spectrometry Mass Spectrometry (SELDI-MS). Hutchens et al. specifically disclose obtaining a sample, exposing the sample to a substrate for use in SELDI-MS that comprises at least one addressable location, each addressable location comprising an adsorbent species such as antibody immoblilized into the substrate, that resolves at least one of the biopolymers under elution conditions, and then subjecting the sample to SELDI-MS. The adsorbent species may also be a biochemical material (metal chelator or anion exchange material) (see column 5, lines 41-43, column 7, lines 11-41, and column 13, lines 47-58). The sample may be unfractionated body fluid such as blood, urine, blood products, i.e. serum, or tissue sample. The method and kit may be applied to multiple samples (see column 8, lines 45-53). The antibody is monoclonal and labeled with a detectable moiety which generates a measurable signal such as radioactive, chromogenic, or fluorescent (see column 15,m line 59 to column 16, line 25). According to Hutchens et

al., SELDI is a solid phase method for desorption of biopolymers wherein the biopolymer is presented to an energy stream on a surface that enhances biopolymer capture or desorption which come in three versions, 1) Surface enhanced affinity capture, 2) Surface enhanced neat desorption, and 3) Surface-enhanced photolabile attachment and release (see columns 24-26).

Hutchens et al. differ from the instant invention in failing to disclose that the biopolymer marker comprises SEQ ID NO. 1.

Capiaumont et al. teaches SEQ ID NO. 1 which is C3f (SSKITHRIHWESASLLR), a fragment of human complement containing HWESAS motif. According to Capiaumont et al., SEQ ID NO. 1 which contains HWESAS is a biopolymer which exhibits, i.e. evidences or categorizes, at least one disease state; in this case, chronic renal failure (see Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teaching of Capiaumont of SEQ ID NO. 1 which comprises a biopolymer used as a diagnostic marker of a disease state, in this case, chronic renal failure, with the method of Hutchens which uses SELDI-MS for differential detection of biopolymers because Hutchens specifically taught using a substrate having an adsorbent capable of resolving distinct biopolymers, including diagnostic markers of a disease state such as chronic renal failure biopolymer marker, i.e. SEQ ID NO. 1 as taught by Capiaumont, for detection by SELDI-MS.

5. No claims are allowed.

Remarks

6. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Hutchens et al. (US 6,020,208) disclose systems containing probes for presenting analytes to an energy source for surface-enhanced affinity capture for SELDI-MS (see column 13 and Examples 4 and 5).

Yates III et al. (US 5,538,897) disclose mass spectrometry fragmentation patterns of peptides to identify amino acid sequences in databases.

WO 87/06344 (Nilsson) discloses antibody preparations directed against an individual neoantigen in the C3b region of human C3 (see pages 1-5).

WO 00/49410 (Liotta et al.) disclose devices and methods for protein analysis on laser capture microdissected cells which permit proteomic analysis on cells from different populations using SELDI-MS.

Thomas et al. (Third component of human complement : Localization of the internal thiolester bond, Proc. Natl. Acad. Sci 79: 1054-1058 (1982)) teach inactivation of human complement protein C3, and amino-terminal sequence of fragment C3d.

Koch et al. (A Novel Polymorphism of Human Complement Component C3 detected by means of a Monoclonal Antibody, Immunogenetics, 23: 322-325 (1996)) teach using mouse Mab, HAV 4-1 having reactivity which is closely related to C3F.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gail Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gail Gabel
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CHRISTOPHER L. CHIN
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